REMARKS

Prior to the present amendment, claims 1, 5, 6, 17-20, and 24-27 were examined. By the present amendment, claims 2, 6, 18, 19 and 21-23 have been canceled without prejudice. Claims 1, 5, 17, 20, and 24-27 are pending in the subject application. Claims 1, 5, 17, 20, 24, 25 and 27 have been amended and support for these amendments are found throughout the specification. Claims 1, 5, 17-18, 20, and 24 have been amended to recite EGFR as the tumor gene determinant. Claims 20 and 27 have also been amended to correct dependency. No new matter is raised by these claim amendments.

Accordingly, claims 1, 5, 17, 20, and 24-27 are presented for examination on the merits.

Objections of the specification

The prior applications were incorporated by reference throughout the specification as filed. *See* for example page 13, 15, 23, and 24. Applicants amended paragraph one of the specification merely for convenience. Addition of the incorporation by reference language in the first paragraph is thus not an addition of new matter. In addition, the specification has been amended to recite the appropriate U.S. Application serial numbers referenced. Accordingly, applicant respectfully requests withdrawal of this ground of objection.

Objection of claims 24, 25, and 27

Claims 24, 25, and 27 are objected to for various reasons including reciting a phrase twice, missing a step-identifier, or referencing non-elected subject matter or for being dependent on claims that were not elected. In view of the current amendments made to the claims or cancellation of claims, the objections are now moot. Accordingly, applicant respectfully requests withdrawal of this ground of objection.

Rejection of claims 1, 5, 6, 7-20 and 24-27 under of 35 U.S.C. §112, Second Paragraph - Written Description

Claims 1, 5, 6, 17-20, and 24-27 stand rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for failing to identifying the claimed method.

The claims have been amended or canceled, thus rendering this ground of rejection moot. Accordingly, applicants request withdrawal of this ground of rejection.

Claims 1 and 17 (and dependent claims 5, and 18-20) stand rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting a conjunction between the steps.

Claims 1 and 17 have been amended, thus rendering this ground of rejection moot.

Accordingly, applicants request withdrawal of this ground of rejection.

Claim 25 (and dependent claims 26 and 27) stand rejected under 35 U.S.C. § 112, second paragraph, for reciting the phrase "said isolated and purified nucleotide" without sufficient antecedent basis and further for the phrase being indefinite.

Claim 25 has been amended, thus rendering this ground of rejection moot.

Accordingly, applicants request withdrawal of this ground of rejection.

Claims 1, 17, 24 and 25 (and dependent claims 5, 6, 18-20, 26 and 27) stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting the phrase "predetermined threshold level for the tumor gene determinant."

Applicants disagree for the following reasons. Throughout the specification, the term "predetermined threshold level" is described in the specification as a statistical correlation of the expression level of a "tumor gene determinant" with the effectiveness of a course of treatment including a "chemotherapeutic agent specific for the tumor gene determinant." *See* for example page 13, line 21- page, 15, line 9. One of ordinary skill in the art would know that by comparing the amount of tumor gene determinant mRNA in the tumor sample to the predetermined threshold level for the tumor gene determinant, one would be able to prognosticate the effectiveness of a course of treatment. In addition, the specification provides various known tests useful to one skilled in the art to determine a threshold level. Finally, several co-pending applications, which are incorporated by reference, also set forth methodologies for determining a threshold value.

Accordingly Applicants respectfully request withdrawal of this ground of rejection.

Rejection of claims 1, 5, 17, 24 and 27 under

of 35 U.S.C. §112, First Paragraph - Written Description

Claims 1, 5, 17, 24, and 27 stand rejected under 35 U.S.C. § 112, first paragraph, on the

grounds that the specification does not enable one of ordinary skill in the art to use the invention commensurate in scope with the claims. In particular, the examiner alleges that the method involves any tumor gene determinant and the specification gives guidance for a small number of genes which would be useful for tumor gene determinant "but not a representative number of genes that would adequately guide/direct one skilled in the art to practice the method in commensurate with the claimed scope."

Applicants disagree for the following reasons. Claims 1, 17 and 24 (and dependent claim 5) now provide the tumor gene determinant is EGFR, thus rendering this ground of rejection moot.

Accordingly Applicants respectfully request withdrawal of this ground of rejection.

Rejection under 35 U.S.C. § 102(e)

Claims 1, 5, and 6 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Kopreski (U.S. Patent No. 6,759,217 B2) ("Kopreski"). The Examiner alleges that Kopreski teaches a method of determining an expression level of mRNA via RT-PCR of EGFR wherein the assay inherently involves the comparison of a housekeeping gene to the marker gene. Applicants respectfully disagree for the following reasons.

The present invention provides a method to determine an appropriate chemotherapeutic regimen for treating a metastic tumor in a patient based upon the level of tumor gene expression from a patient derived primary tumor sample. Kopreski does not teach determining an appropriate chemotherapetic regimen for treating a metastic tumor. The cited reference merely teaches a method for detecting EGF RNA in bodily fluids. (See column 2, lines 31-44). Furthermore, unlike Kopreski, the present invention is not limited to a sample that is bodily fluid. Furthermore, the cited reference does not disclose or teach a method of that involves a "primary tumor sample" as well as a "predetermined threshold level." Applicants submit that the cited reference does not teach nor suggest the present invention for these reasons and that the claims are not anticipated by Kopreski. Accordingly, applicants request withdrawal of this ground of rejection.

Rejection under 35 U.S.C. § 103(a)

Claims 17, 18, and 24 stand rejected under 35 U.S.C. § 103(a) as being obvious over

Kopreski (U.S. Patent No. 6,759,217 B2) ("Kopreski") in view of Danenberg et al. (U.S. Patent NO. 6,248,535 B1). The Examiner alleges that Kopreski teaches a method of determining an expression level of mRNA via RT-PCR of EGFR wherein the assay inherently involves the comparison of a housekeeping gene to the marker gene.

In accordance with MPEP §706.02(I)(1), at the time the invention was made, the subject matter to the '535 patent and the claimed invention was owned by the same corporation, Response Genetics, Inc. Therefore, the disclosure, the '535 patent, is not an invention "by another." Accordingly, applicants request withdrawal of this ground of rejection.

Double Patenting

Claims 1, 5, 6, 17-20, and 24-27 stand rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,582,919 B2 (the '919 patent). Applicants disagree. The current application is directed to a method of determining a chemotherapeutic treatment in a patient with a metastic tumor based on the mRNA expression of a tumor gene determinant, namely EGFR, in a primary tumor sample. The '919 patent does not disclose or claim a method that addresses determining a chemotherapeutic treatment of metastic tumors in patients based on EGFR expression in a primary tumor sample from that patient. Therefore, the current application is patentably distinct. Accordingly, withdrawal of this provisional rejection is respectfully requested.

CONCLUSION

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 11-0600.

The Examiner is invited to contact the undersigned at 202/220-4258 to discuss any matter in this application.

Respectfully submitted,

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